

illness, particularly cardiac arrest from coronary artery disease. Of the 650,000 people who die of arteriosclerotic heart disease annually (primarily from coronaries), upgrading the training of ambulance personnel from emergency medical technician to paramedic service has resulted in a 10 percent increase in survival (that is, of 100 cardiac arrests, an additional 10 lives have been saved, an improvement from 7 percent to 17 percent). In cardiac arrest from coronary artery disease, an ambulance response time of less than two minutes will allow 55 percent of patients to be admitted to hospital, whereas if the response time is eight minutes, only 19 percent will survive long enough to be admitted to hospital. The comparable discharge survival data are 33 percent and 12 percent, respectively. The improvement in survival of a cardiac arrest victim from coronary artery disease has been in the range of 10 percent. Because about 25 percent of these patients sustain cardiac arrest acutely, the net potential benefit of prehospital care is an improvement in survival of 2.5 percent ( $25 \times 10$ ) of all cardiac arrest victims.

Extrapolation of data on cases of cardiac arrest from coronary artery disease to trauma cases is inappropriate. Although it is attractive to assume that more training and utilization of on-site equipment such as pneumatic antishock garments (military antishock trouser, or MAST suits) should produce improvement in the care of patients with severe injury, no data exist to prove this thesis. Information is beginning to emerge that establishes that transport delays for purposes of on-site resuscitation are associated with excessive mortality if the injury is life threatening. For example, in one study evaluating traumatic injury to the heart, there were no survivors among patients in whom field resuscitation with concomitant prolonged prehospital delay occurred. If prompt transport of victims with heart wounds occurs, a 20 percent to 30 percent survival is possible. Similar findings for other types of severe injuries associated with hemorrhagic shock are applicable when the availability of prompt and appropriate care is within a 15- to 20-minute transport time. In patients with less acute but equally life-threatening injuries, a "golden interval"—usually less than an hour—is best spent in transportation to a trauma center after stabilization of fractures and initiation of intravenously given fluid therapy.

Maximal use of the first hour after injury depends on geographic considerations. In areas of dense population with short distances to a trauma care center, such as in San Francisco, ground transportation is the optimal transport means. In rural areas, such as the Imperial Valley (south central California), rotary or fixed-wing transport to a trauma care center has resulted in a substantial improvement in mortality for injuries of comparable magnitude, when victims are rapidly moved to definitive care, rather than receiving initial extensive prehospital and "nearest hospital" care.

Studies done in California and elsewhere speak to the need for continued definition of a regional system

of trauma care, as defined by the report "Categorization of Emergency Facilities and Trauma Centers" by the Committee on Trauma of the American College of Surgeons. Several studies have shown that 30 percent to 35 percent of trauma deaths are potentially salvageable, if treated in a trauma center. The absence of a system for transportation and care of trauma victims and the persistence of the "nearest hospital" concept continue to result in unnecessary death after injury. The increasing tendency for transport delay for purposes of extensive field resuscitation is contributing to this problem.

Because about 5 percent of motor vehicle injuries are critical, a system to minimize the death rate from such injuries is necessary. Because as high as 50 percent of deaths from injury occur *after* the patients reach the hospital, continual evolution of trauma care centers, appropriate prehospital care, proper transportation systems and development of new trauma care centers are mandatory.

It is now apparent that trauma care centers can improve mortality from injury. Because transportation systems are available to bring patients to a trauma care center, emphasis should be placed on rapid transport and not on field resuscitation.

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## Parathyroid Autotransplantation

THE SUCCESS AND SIMPLICITY of parathyroid autotransplantation favors the use of this technique in standard surgical practice for those patients who stand to lose all parathyroid function as a consequence of a neck exploration or in whom residual or in situ parathyroid tissue has a good likelihood of becoming hyperactive. The principles of parathyroid transfer are the same as those for other grafts without a vascular pedicle such as a split-thickness skin graft in that the graft will be profoundly ischemic until capillary perfusion begins in three to five days. During this time the tissue is nourished by diffusion only. The graft will succumb to ischemia if vascular ingrowth is delayed by such factors as low perfusion pressure, regional scar, hematoma or infection. However, a split-thickness skin graft is prepared to function as an epithelium within 10 to 14 days of grafting while the endocrine epithelium of parathyroid tissue temporarily loses function during the three to five days when only diffusion is providing metabolic exchange. This diffusion support is only adequate for subsequent survival if the parathyroid graft is reduced to fragments no larger than 1 to 2 mm in diameter. The subsequent function of the graft will not be evident

until the endocrine epithelium has been regenerated on the interstitial matrix. This may take as long as three months. If the patient is dependent on the graft, calcium and vitamin D supplementation are required during the accommodation phase of engrafting.

Dr Sam Wells of Washington University (St Louis) has accumulated the largest number of cases of parathyroid grafting and a review of his series clarifies the indications for the procedure. Patients who have multiple endocrine adenopathy or secondary hyperparathyroidism have a high rate of recurrence and therefore reexploration procedures of the neck. The hazards of repeat neck operations are well recognized and can be avoided by removing all parathyroid tissue from the neck at the time of the first exploration. Patients who must have a repeat neck exploration can present even greater difficulty in identifying normal parathyroid tissue than in locating the abnormal tissue causing the recurrent or persistent disease. The risk of permanent hypoparathyroidism is best managed by transplanting 30 mg of parathyroid tissue to a site more accessible than the paratracheal region. Patients who require a total thyroidectomy for carcinoma have always been at risk for hypoparathyroidism because the blood supply to the thyroid gland is shared by the parathyroids and wide excision for thyroid carcinoma can destroy the parathyroids by infarction. This potential parathyroid loss is well managed by autotransplantation. The following are clear indications for parathyroid autotransplantation: (1) multiple endocrine adenopathy and (2) secondary hyperparathyroidism because of high likelihood of recurrence; (3) reexploration of the neck, and (4) total thyroidectomy because of the risk of hypoparathyroidism.

The grafting technique is not difficult. The parathyroid tissue is finely minced to 1-mm fragments for grafting. About 30 of these fragments are transferred to the brachioradialis muscle. Pockets are created among the muscle fascicles and after careful hemostasis four to five tissue fragments are placed in each. The muscle is closed, with each site marked with a non-absorbable suture. An interesting feature is that the transplanted tissue need not be *normal* parathyroid. Hyperplastic tissue has shown little tendency to excessive function if no more than 30 mg is transplanted. The function of the graft is monitored by comparing the parathormone levels in the antecubital vein of the grafted and the ungrafted arms. After two months the parathormone level usually suggests function and the vitamin D and calcium support can be sequentially withdrawn. Autotransplantation was successful in 92 percent of the patients of Wells and colleagues who had primary hyperparathyroidism and in all patients managed for total thyroidectomy. Cryopreservation of parathyroid tissue has been extremely useful, such that an inadequate graft can be supplemented with preserved autologous tissue. Rarely, the graft will release excessive parathormone and this can be corrected by removing two to three of the pockets of transplanted

tissue. The excision can be conducted under local anesthesia in an outpatient setting.

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### Adrenalectomy for Metastatic Breast Cancer: Surgical Versus Medical Treatment

ONE OF THE MOST IMPORTANT FACTORS associated with an improved prognosis in metastatic breast cancer is the presence of estrogen-receptor protein in the tumor cell cytoplasm. Some 50 percent to 60 percent of patients with estrogen-receptor-positive tumors respond to oophorectomy or to antiestrogen therapy such as the administration of tamoxifen citrate. In addition to the presence of estrogen receptors, additional factors that affect a favorable prognosis include a long disease-free interval, a good response to previous endocrine therapy and metastatic tumor involvement limited to soft tissue and bone. Of women who have responded to oophorectomy or antiestrogen treatment, 30 percent to 40 percent will respond to a subsequent surgical adrenalectomy.

Aminoglutethimide is a compound that was initially developed as an anticonvulsant and later found to be an inhibitor of adrenal steroid production. Aminoglutethimide blocks the conversion of cholesterol to  $\Delta^5$ -pregnenolone at the beginning of the biosynthetic pathway, blocking the production of cortisol, androgens, estrogens and aldosterone. There is an additional blocking of estrogen in the peripheral tissues by the inhibition of androstenedione conversion to estrone and estradiol. With suppression of the adrenal gland, there is a fall in cortisol levels and a rise in adrenocorticotrophic hormone level that can overcome the aminoglutethimide blockade unless a glucocorticoid is also given. Most patients will have maximal estrogen suppression with administration of aminoglutethimide, 250 mg given by mouth four times a day, together with 40 mg of hydrocortisone in divided doses (10 mg in the morning, 10 mg in the afternoon and 20 mg at bedtime). Due to occasional salt-loss problems, supplementation with a mineralocorticoid (fludrocortisone acetate, 0.1 mg given twice weekly) may be required, particularly during hot weather. Early side effects with the drug are common but usually subside in two to three weeks. The side effects are ataxia, lethargy, dizziness, visual blurring and a pruritic maculopapular rash. These side effects usually do not warrant an alteration in medication because they tend to be self-limited. Occasional cases of hypothyroidism have been described, as have rare blood dyscrasias.

The medical adrenalectomy regimen of aminoglutethimide plus glucocorticoids in a study of 50 postmenopausal patients with metastatic breast cancer showed a